“Task-shifting” for HIV Care

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 Associate Professor Internal Medicine and Infectious Diseases
 University of the Witwatersrand
 CEO Right to Care
The human resources crisis:

Health care personnel (doctors and nurses) per 100,000 population

<table>
<thead>
<tr>
<th></th>
<th>South Africa</th>
<th>Botswana</th>
<th>Ghana</th>
<th>Tanzania</th>
<th>Malawi</th>
<th>USA</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doctors</td>
<td>69.2</td>
<td>28.7</td>
<td>9.0</td>
<td>2.3</td>
<td>1.1</td>
<td>230</td>
<td>256</td>
</tr>
<tr>
<td>Nurses</td>
<td>388</td>
<td>241</td>
<td>64</td>
<td>113</td>
<td>36.6</td>
<td>1212</td>
<td>937</td>
</tr>
</tbody>
</table>

Addis Abba Declaration Jan 2008

• Africa qualifies 5100 doctors per year
• Americas qualify 68,500 per year

REF: Task Shifting to tackle health worker shortage WHO/HSS/2007.03
Definition of “Task-Shifting”

“...a process of delegation whereby tasks are moved, where appropriate, to less specialized health workers. By reorganizing the workforce in this way, task shifting can make more efficient use of the human resources currently available. For example, when doctors are in short supply, a qualified nurse could often prescribe and dispense antiretroviral therapy. Further, community workers can potentially deliver a wide range of HIV services thus freeing the time of qualified nurses. Training a new community health worker takes between one week and one year depending on the competencies required. This compares with three or four years of training required for a nurse to fully qualify.”

REF: Task Shifting to tackle health worker shortage WHO/HSS/2007.03
Definition of “Task-Shifting”

Dispensing Nurses

Pharmacy Assistants

Administrative Assistants

Pharmacist

Central Pharmacy

Central Procurement Tender

Central Pharmacy Stores

Distribution

Hospital

District Stores

Pharmacy Facilities

Pharmacy Assistant

PHC Facility

Dispensing Nurses

REF: Ian’s Modification for Pharmacy Personnel
Sequencing Pragmatic and Explanatory Trials


“The pragmatic attitude favours design choices that maximize applicability of the trial’s results to usual care settings, rely on unarguably important outcomes such as mortality and severe morbidity, and are tested in a wide range of settings.”

Zwarenstein M et al. BMJ 2008;337:a2390
Summary of Presentation

- Randomized clinical trial
- Cluster Randomized Trial
- Implementation research
- Pharmacy programme
- Regulatory environment
- Closing
Nurse versus doctor management of HIV-infected patients receiving antiretroviral therapy (CIPRA-SA): a randomised non-inferiority trial

Ian Sanne, Catherine Orrell, Matthew P Fox, Francesca Conradie, Prudence Ihe, Jennifer Zeinecker, Morna Cornell, Christie Heiberg, Charlotte Ingram, Ravindra Panchia, Mohammed Rassool, René Gonin, Wendy Stevens, Handré Truter, Marjorie Dehlinger, Charles van der Horst, James McIntyre, Robin Wood, for the CIPRA-SA Study Team*

Lancet 2010; 376: 33-40

This online publication has been corrected. The corrected version first appeared at TheLancet.com September 24, 2010

Published Online June 16, 2010
DOI:10.1016/S0140-6736(10)60894-X

Guideline regimens: D4T, 3TC, NVP or EFV
AZT, DDI, LPV/rit

Screening for eligibility criteria by a CIPRA safety team

Eligible (INDEX PATIENT) Household randomization

Regimen 1

Doctor Monitored Treatment

Treatment failure

Regimen 2

Nurse Monitored Treatment

Treatment failure

Regimen 2
Objective, study population

- To demonstrate that a first line antiretroviral therapy regimen, administered at a primary health care level monitored by sisters (investigative arm), is not inferior to a doctor monitored treatment (standard/control arm), as measured by cumulative treatment failure rate.

- Inclusion criteria
  - Adults >16 yrs
  - CD4 + <350 and or WHO 3 and 4 AIDS defining illness

- Exclusion criteria
  - Current active OI
  - Use of prior HAART (excluding MTCT)

- 80% power to demonstrate a 1.40 difference
## Randomisation

<table>
<thead>
<tr>
<th></th>
<th>Nurse Arm</th>
<th>MO Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female</strong></td>
<td>297</td>
<td>273</td>
</tr>
<tr>
<td><strong>Age</strong> median years (IQR)</td>
<td>32.3 (28.0-36.6)</td>
<td>32.2 (28.0-37.4)</td>
</tr>
<tr>
<td><strong>BMI</strong> (kg/m$^2$), median (IQR)</td>
<td>23.5 (21.3-27.6)</td>
<td>23.5 (20.4-26.8)</td>
</tr>
<tr>
<td><strong>CDC Classification</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class A (%)</td>
<td>159 (39.4%)</td>
<td>140 (34.4%)</td>
</tr>
<tr>
<td>Class B (%)</td>
<td>110 (27.2%)</td>
<td>117 (28.8%)</td>
</tr>
<tr>
<td>Class C (%)</td>
<td>134 (33.2%)</td>
<td>150 (36.8%)</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>1 (0.2%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td><strong>CD4 Count (cell/mL )</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 200 (%)</td>
<td>260 (64.4%)</td>
<td>257 (63.1%)</td>
</tr>
<tr>
<td>200 - 350 (%)</td>
<td>119 (29.5%)</td>
<td>130 (31.9%)</td>
</tr>
<tr>
<td>350 - 500 (%)</td>
<td>23 (5.7%)</td>
<td>18 (4.4%)</td>
</tr>
<tr>
<td>&gt;500 (%)</td>
<td>2 (0.5%)</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>157 (100-230)</td>
<td>161 (105-218)</td>
</tr>
<tr>
<td><strong>Viral load (copies/mL)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;= 100,000 (%)</td>
<td>181 (44.8%)</td>
<td>169 (41.5%)</td>
</tr>
<tr>
<td>&gt; 100,000 (%)</td>
<td>223 (55.2%)</td>
<td>238 (58.5%)</td>
</tr>
<tr>
<td>Log mean viral load (Std Dev.)</td>
<td>5.09 (0.75)</td>
<td>4.99 (0.73)</td>
</tr>
</tbody>
</table>
## ART Regimens Table 2

<table>
<thead>
<tr>
<th>Assigned regimens</th>
<th>Nurse Arm</th>
<th>MO Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Percent</td>
</tr>
<tr>
<td>D4T+3TC+EFV (%)</td>
<td>293</td>
<td>(72.5 %)</td>
</tr>
<tr>
<td>D4T+3TC+NVP (%)</td>
<td>72</td>
<td>(17.8 %)</td>
</tr>
<tr>
<td>D4T+3TC+LPV/r (%)</td>
<td>35</td>
<td>(8.7 %)</td>
</tr>
<tr>
<td>D4T+3TC+NFV (%)</td>
<td>4</td>
<td>(1.0 %)</td>
</tr>
</tbody>
</table>
Primary analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Medical Officer</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CUMULATIVE FAILURE</td>
<td>192/404 (47.5%)</td>
<td>179/408 (43.9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Nurses are non-inferior to doctors in monitoring first line ART treatment in treatment naïve HIV-1 infected patients
- CI boundary within HR < 1.40 as set in the protocol
### Failure Criteria by Study Arm Table 3.

<table>
<thead>
<tr>
<th></th>
<th>Primary Health Care Nurse (N=404)</th>
<th>Clinical Nurse Officer (N=408)</th>
<th>Hazard Ratio (95% CI)</th>
<th>Favors PHCN Arm</th>
<th>Favors CO Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CUMULATIVE FAILURE</strong></td>
<td>192 (48%)</td>
<td>179 (44%)</td>
<td>1.09 (0.89-1.33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Virologic Failure</td>
<td>44 (11%)</td>
<td>39 (10%)</td>
<td>1.15 (0.75-1.76)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1.5 Log drop VL^</td>
<td>7 (2%)</td>
<td>6 (2%)</td>
<td>1.18 (0.40-3.51)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 VL &gt; 1000*</td>
<td>37 (9%)</td>
<td>33 (8%)</td>
<td>1.14 (0.71-1.82)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Toxicity Failure</strong></td>
<td>68 (17%)</td>
<td>66 (16%)</td>
<td>1.04 (0.74-1.45)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Loss**</td>
<td>70 (17%)</td>
<td>63 (15%)</td>
<td>1.13 (0.81-1.59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Withdrew Consent</td>
<td>18 (5%)</td>
<td>21 (5%)</td>
<td>0.87 (0.46-1.63)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Default Clinic Schedule</td>
<td>38 (9%)</td>
<td>32 (8%)</td>
<td>1.21 (0.76-1.93)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lost to follow up</td>
<td>14 (4%)</td>
<td>10 (3%)</td>
<td>1.42 (0.63-3.20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>10 (3%)</td>
<td>11 (3%)</td>
<td>0.92 (0.39-2.17)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*VL: Virological Load; ^Log: logarithmic; *: p<0.05; **: p<0.01
Log rank p value = 0.4238

Time to Failure by Treatment Arm

- Nurse
- Medical Officer

N - (Event)

Nurse 404 (83) 319 (78) 235 (26) 61 (4) 0
Medical Officer 408 (81) 325 (73) 243 (19) 66 (3) 0
Toxicity Failures

• Protocol mandated end point if the following criteria were met
  – >42 days Treatment interruption due to Grade 3 or 4 adverse drug reaction
  – ACTG toxicity tables were modified during the study including lactate
  – After DSMB in June 2007, the grading of hyperlactataemia was changed with retraining at sites.
HIV treatment outcomes

Treatment CD4+ count gain
Proportion viral load undetectable <50c/ml

- Modified intention to treat
- No difference in the treatment efficacy
- Increased recognition of Respiratory, Cardiovascular and Peripheral Neuropathy adverse events
Time to Failure by Baseline VL/ARM

- Doctor - VL < 100,000
- Doctor - VL >= 100,000
- Nurse - VL < 100,000
- Nurse - VL >= 100,000

Treatment Failure

0.00 0.25 0.50 0.75 1.00

0 12 24 36 48

Months

P = 0.0865
Initiating patients on antiretroviral therapy at CD4 cell counts above 200 cells/µl is associated with improved treatment outcomes in South Africa

Fox, Matthew Pa,b,c,d; Sanne, Ian Mc; Conradie, Francescae; Zeinecker, Jenniferf; Orrell, Catherinee; Ive, Prudencee; Rassool, Mohammede; Dehlinger, Marjorief; van der Horst, Charlesg; McIntyre, Jamesh; Wood, Robin"
Summary of Presentation

- Randomized clinical trial
- Cluster Randomized Trial
- Implementation research
- Pharmacy programme
- Regulatory environment
- Closing
### Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial

Lara Fairall, Max O Bachmann, Carl Lombard, Venessa Timmerman, Kerry Uebel, Merrick Zwarenstein, Andrew Boulle, Daniella Georgeu, Christopher J Colvin, Simon Lewin, Gill Faris, Ruth Cornick, Beverly Draper, Mvula Tshabalala, Edvan Kotze, Cloete van Vuuren, Dewald Steyn, Ronald Chapman, Eric Bateman

<table>
<thead>
<tr>
<th>QUESTION</th>
<th>PARTICIPANTS</th>
<th>PRIMARY OUTCOME</th>
<th>DESIGN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse-led service as effective as a doctor-led one for patients on ART?</td>
<td>On ART ≥ 6 months</td>
<td>Viral load suppression</td>
<td>Equivalence</td>
</tr>
<tr>
<td>Improve on status quo, expanding access and reducing “waiting list” mortality?</td>
<td>CD4 ≤350 not yet on ART</td>
<td>Time to death</td>
<td>Superiority</td>
</tr>
</tbody>
</table>
STRETCH

Streamlining Tasks and Roles to Expand Treatment and Care for HIV

Educational outreach training using PALSA PLUS model

Change facilitator: STRETCH provincial co-ordinator

Participatory action approach to re-organisation of care:
• Local facility management teams
• STRETCH toolkit
• Phased introduction

Uebel K et al. Implementation Science 2011;6(1) 86
Results: STRETCH

• Similar treatment outcomes, VL suppression, no improvement in survival

• No difference in the % started on ART
• Improvements in proportion of patients on ART CD4+ 200-350
• started at the same mean ART=132 cells/mm3
Cohort 1 (CD4 ≤ 350 not yet on ART) Primary outcome

HR 0.92 (95% CI 0.76 – 1.15; p 0.532)

CD4 count ≤ 200
HR 1.00 (95% CI 0.52 – 1.00; p 0.020)

CD4 count 201-350
HR 0.73 (95% CI 0.54 – 1.00; p 0.052)

Interaction term p 0.050
The context of the STRETCH trial
26%  
Proportion of intervention group patients started on ART who were initiated by a nurse

Why so low?

Didn’t intend for nurses to start 100% who needed treatment
Context not always supportive (“breaking the law”)
Initiation more complex than re-prescribing
Clinical confidence grew slowly
Tendency to defer to doctors if available
Tendency to practise as a collective
Moratorium on ART initiations

Effect of moratorium on ART initiations

No. ART initiations per month since start of trial (moratorium during months 11-14)
Streamlining Tasks and Roles...
but *not* drug distribution!
Lesson 1

Nurses are safe
Lesson 2

Number of initiating sites more important than number of initiators
Lesson 3

Nurses practise collectively and follow guidelines
Lesson 4

There are other obstacles to scale-up
Lesson 5

“The nurses can do everyone’s job, but no one can do the professional nurse’s job. That is a problem, so we are overloaded. We are really exhausted.”

Task-shifting has ripple effects
Summary of Presentation

- Randomized clinical trial
- Cluster Randomized Trial
- Implementation research
- Pharmacy programme
- Regulatory environment
- Closing
To evaluate this strategy, we compared doctor initiated patients eligible for nurse management who received either:

- Doctor management (N=1620)
- Nurse management (N=540)

Conducted a retrospective cohort study

Matched on age, gender, CD4 count, time on ART, and regimen using propensity scores
Figure 1. Decision process for assigning HIV treatment outcomes. Patients were placed in a mutually exclusive patient outcome category 12 mo after study enrolment – no longer in care, in care and responding or in care and not responding. Patient outcomes were defined based on the patient’s vital status, presence in the clinic, viral load or CD4 count at 12 mo after study enrolment. For those patients alive and in treatment, viral load was the preferred outcome indicator, but in the absence of viral load CD4 count was used and if neither were available then it was assumed the patient was in care and responding based on their presence in the clinic. The diagnostic result closest to 12 mo, but within 3 mo (9–15 mo) was used. doi:10.1371/journal.pmed.1001053.g001
## Results: Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nurse managed</th>
<th>Doctor managed</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>540</td>
<td>1620</td>
</tr>
<tr>
<td>Mean age at study enrolment (years)</td>
<td>38.7</td>
<td>38.9</td>
</tr>
<tr>
<td>Median CD4 count at ART initiation (cells/mm³)</td>
<td>103</td>
<td>94</td>
</tr>
<tr>
<td>Median CD4 count at study enrolment (cells/mm³)</td>
<td>393</td>
<td>384</td>
</tr>
<tr>
<td>Mean duration on ART at study enrolment (months)</td>
<td>13.2</td>
<td>13.2</td>
</tr>
<tr>
<td>ARV regimen at study enrolment (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D4T-3TC-EFV</td>
<td>67.4</td>
<td>66.9</td>
</tr>
<tr>
<td>AZT-3TC-EFV</td>
<td>27.2</td>
<td>26.9</td>
</tr>
<tr>
<td>Other</td>
<td>5.4</td>
<td>6.2</td>
</tr>
</tbody>
</table>
## Results 2 – 12 Month Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Number events (n, %)</th>
<th>Rates / 100 pyrs</th>
<th>Crude RD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loss to follow-up</strong> (defined as having not attended the clinic in four months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nurse managed</td>
<td>12 (1.7%)</td>
<td>1.7</td>
<td>0</td>
</tr>
<tr>
<td>Doctor managed</td>
<td>94 (4.4%)</td>
<td>4.6</td>
<td>2.7% (1.4%-4.0%)</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nurse managed</td>
<td>1 (0.14%)</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>Doctor managed</td>
<td>24 (1.1%)</td>
<td>1.2</td>
<td>1.0% (0.5%-1.5%)</td>
</tr>
<tr>
<td><strong>Viral load rebound</strong> (unsuppressed ≥400 copies/mL by 12 months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nurse managed</td>
<td>22 (3.1%)</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Doctor managed</td>
<td>102 (4.8%)</td>
<td>-</td>
<td>2.4% (0.7%-4.1%)</td>
</tr>
</tbody>
</table>

### Difference

<table>
<thead>
<tr>
<th>Difference (95% CI)</th>
<th>Difference in mean CD4 response (cells/mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse vs. Doctor</td>
<td>-7 (-19.3-5.0)</td>
</tr>
</tbody>
</table>
Results 4: Cost Breakdown

• Treatment outcomes in care and responding nurse vs. doctor 95% vs. 89%
• $67/ann. cost
Summary of Presentation

- Randomized clinical trial
- Cluster Randomized Trial
- Implementation research
- Pharmacy programme
- Regulatory environment
- Closing
Pharmacy programme

- Procurement success
- Pharmacy management systems
- Pharmacy Assistants (register closes 2017)
- Pharmacy Technicians (first training 2013)
- District Pharmacy Systems
Scope of practice
Regulatory environment

• Pharmacy regulations
• Nursing council
• Health Professionals Council

• Community Health Care Workers
• Pharmacy Technicians
• Primary Health Care Nurses
Conclusions

• Task-shifting may be facilitated by guideline changes:
  – Less toxic treatment regimens
  – Fixed dose combinations
    • TDF, FTC, EFV
    • AZT, 3TC, ATV/r
  – Higher CD4+ count
  – Simplified laboratory monitoring schedule
Conclusions

• Nurses are the backbone of the health system and are equivalent to doctors in managing HIV
• Pharmacy programmes depend on task-shifting
• Training and capacity is limited by the scope of practice discussions (HPCSA, Nursing Council, Pharmacy Council)
• Health system decisions require more dedicated planning and a responsive regulatory environment
Acknowledgements

Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial

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Lara Fairall and the STRETCH TEAM
Acknowledgements

Wits University
Prudence Ive
Patrick MacPhail
Francesca Conradie
Cindy Firnhaber
Liesl Page-Shipp
Mhairi Maskew
Lawrence Long
Denise Evans
UCT – Desmond Tutu HIV Research Center
Robin Wood
Lind-Gail Bekker
Catherine Orrell
Jennifer Zeinecker
HEERO – Boston University
Sydney Rosen
Mathew Fox
Gesine Meyer-Rath
Jonathan Simone
Kate Bistline

National Health Laboratory Services
Wendy Stevens
Carole Wallis

Department of Health
Gauteng Department of Health
National Department of Health

Right to Care/USAID
Melinda Wilson
Kurt Firnhaber
Thembi Xulu

NIH/ Division of AIDS
Carolyn Williams
Donna Germuga

TherapyEdge
Chalom Sayada
Ronan Boulme
Acknowledgements